**REMARKS**

Claims 41, 42 and 44-82 presently appear in this case. Claims 65, 66, 79 and 80 have been objected to but have been indicated to be allowable if rewritten into independent form (although claim 79 is already independent). The official action of June 8, 2005, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to the therapeutic use of an A3-selective adenosine A3 receptor agonist (A3RAg), in an effective amount that assures selectivity, for inhibiting abnormal cell proliferation, including the treatment of cancer, and for inducing G-CSF production or secretion. The effective amount is preferably less than 100 μg/Kg body weight such that it exerts its prime effect through the A3 adenosine receptor without essentially activating adenosine receptors other than the A3 adenosine receptor.

The examiner-initiated telephone conference of May 19, 2005, is hereby gratefully acknowledged. In this interview, the examiner stated that he still read claim 41 so broadly as to read on the prior art. The examiner suggested, however, that the claims would be in condition for allowance if the amount administered, from claim 79, were inserted into the broadest claims. The undersigned advised the examiner that he would check with the client and again contact the examiner to advise him whether such amendment would be accepted.

The telephone interview initiated by the undersigned on May 24, 2005, is also gratefully acknowledged. In this interview, the examiner was advised that applicant would accept the proposed language for claim 41, but the examiner was queried about whether the same language would have to be added to claims 50 and 57. The examiner stated that claim 50 also required the same language, as did claim 57. The undersigned explained why applicant did not believe that claim 57 required this feature in order to be allowable in view of the recitation that there is essentially no activation of other receptors, particularly in light of the evidence of record that the amounts administered by Kohno will activate other receptors. The undersigned advised that he would discuss the examiner's requested changes to claim 50 and 57 with the client and get back to him. Unfortunately, before the undersigned could again discuss this case with the examiner the official action had already been written.

Claims 41, 42 and 46-49 have been rejected under 35 U.S.C. §102(b) as being anticipated by Kohno. The examiner considers the manipulative operations to be the same.

In order to obviate this rejection, claim 41 has now been amended to specify that the amount administered is less than 100 μg/Kg body weight, and to specify that the method is for "selectively" inhibiting abnormal cell proliferation. It is noted that the examiner has indicated claims 65 and 79, which specify that the active ingredient is administered at an amount less than 100 μg/Kg body weight, as being allowable.

Furthermore, in the interview of May 19, 2005, the examiner suggested that the claims would be allowable if the limitation "the amount being less than 100 μg/Kg body weight" were inserted. The indication of the allowability of those claims presently in the case with this feature indicates that the examiner still believes that the claims would be allowable if this were added. Accordingly, claim 41 has now been amended to specify the amount administered is less than 100 μg/Kg body weight, and this is a specific manipulative difference between claim 41 and Kohno. Accordingly, claim 41 and all those claims dependent therefrom should now be considered to be in condition for allowance. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 41, 42 and 44-49 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Kohno in view of Jacobsen for reasons similar to those discussed above with respect to the anticipation rejection over Kohno.

The insertion of the maximum amount of A3RAg administered in claim 41 obviates this rejection for the same reason discussed above as to why it obviates the anticipation rejection over Kohno.

Furthermore, as previously argued, for example, in applicant's amendment of January 8, 2004, see particularly, pages 66-70, Kohno is talking about apoptosis that can affect all cells. At the concentrations used by Kohno, A3RAg induces apoptosis in all types of cells, normal as well as tumor cells. Thus, Kohno teaches that high concentrations of A3RAg

cause apoptosis, but only showed it on tumor cells, and was silent about occurrence in non-cancer cells. Therefore, Kohno does not teach selective inhibition of tumor cells. The present invention, on the other hand, teaches inhibition of proliferation (rather than apoptosis) of cancer cells using an agonist that specifically interacts with the A3 adenosine receptor. For the prime effect to be mediated through the A3 adenosine receptor, the level of administration is invariably such as not to activate other adenosine receptors, and this has now been made explicit in the present claims either by insertion of specific amounts or by specifying that the level of administration is such so as not to activate other adenosine receptors. Accordingly, reconsideration and withdrawal of this rejection are also respectfully urged.

Claims 41, 42 and 44-56 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Kohno and Can-fite in view of Jacobson. The examiner's reasons why applicant's arguments were not convincing are the same as those discussed above with respect to the previous two rejections. Accordingly, it is believed that the amendment to claim 41 discussed above must obviate this rejection for the same reason that it obviates the other two. Kohno does not teach or make obvious the use of such a small amount of A3RAg and none of the secondary references supply this deficiency. Reconsideration and withdrawal of this rejection are therefore also respectfully urged.

Claims 57-64 and 67-78 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Kohno and Can-Fite in view of Jacobson. The examiner states that Kohno teaches that A3RAg induces apoptosis in HL-60 human promyelocytic leukemia cells and therefore have therapeutic value in the treatment of leukemia. The examiner states that the secondary reference make obvious that which is not taught by Kohno, i.e., that it can be administered orally or in combination with a chemotherapeutic drug or that such receptor agonists would be able to counter the toxic side effects of a chemotherapeutic drug or would have a strong synergistic effect with such chemotherapeutic drug. This rejection is respectfully traversed.

Claim 57 differs from claim 41 in explicitly stating that an amount of A3RAg is administered in a manner such that it exerts its prime effect through the A3 adenosine receptor "without essentially activating adenosine receptors other than the A3 adenosine receptor." This claim recitation distinguishes the method from that of Kohno in the same manner that the recitation of an amount being less than 100 μg/Kg body weight distinguishes from Kohno. The declarations of record establish that the amounts administered by Kohno will essentially activate adenosine receptors other than the A3 adenosine receptor. This is a manipulative difference to the same extent that the amount recited in allowable claim 65 is a manipulative difference. No claim limitation can be ignored. The examiner has not explained why Kohno anticipates this

recitation when the evidence of record clearly establishes that the amount of A3RAg is administered by Kohno in a manner such that it does essentially activate adenosine receptors other than the A3 adenosine receptor. Accordingly, regardless of whether Can-Fite and Jacobson make obvious oral administration or in combination with a chemotherapeutic drug, no combination of these secondary references with Kohno can make obvious claim 57 because of this significant difference between the amounts administered by Kohno and the amounts required by the present claims.

Furthermore, claim 57 is limited to a method for selectively inhibiting abnormal cell proliferation, i.e., only killing abnormal cells and not all cells as in apoptosis. Accordingly, reconsideration and withdrawal of this rejection with respect to claim 57 and those claims dependent therefrom are also respectfully urged.

It should be noted that in preparing this amendment it was noted that there could be some ambiguity in the reading of claim 50. Accordingly, applicant has now amended claim 50 in order to clarify it. It is submitted that this amendment should be entered after final because it places claim 50 into better form for either appeal or allowance by inserting antecedent basis for the chemotherapeutic drug treatment referred to on the last line thereof.

New claims 81 and 82 have now been added, dependent respectively from claims 41 and 57, to specify that the abnormal cell proliferation referred to in those claims is

abnormal cell proliferation associated with an autoimmune disease. Support for these claims can be found on page 23, line 15. As claims 41 and 57 have been shown to be allowable herein and as claims 81 and 82 are merely dependent claims adding a feature clearly supported in the specification and therefore not requiring any further substantive examination, it is respectfully requested that they be entered at this stage of the prosecution.

It is submitted that that all the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. §112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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